

SEQUENCE LISTING

<110> NAKAGAWARA, Akira
OZAKI, Toshinori

<120> METHOD OF SCREENING COMPOUND CAPABLE OF ACCELERATING OR INHIBITING
APOPTOSIS, APOPTOSIS ACCELERATOR AND APOPTOSIS INHIBITOR

<130> Q97365

<150> JP 2004-93,266

<151> 2004-03-26

<150> JP 2004-176,107

<151> 2004-06-14

<160> 26

<170> PatentIn version 3.1

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35 40 45

Glu Leu Ser Thr Lys Asn Arg Glu Arg Trp Cys His Glu Ile Gln Ile
50 55 60

Met Lys Lys Leu Asn His Ala Asn Val Val Lys Ala Cys Asp Val Pro
65 70 75 80

Glu Glu Leu Asn Ile Leu Ile His Asp Val Pro Leu Leu Ala Met Glu
85 90 95

Tyr Cys Ser Gly Gly Asp Leu Arg Lys Leu Leu Asn Lys Pro Glu Asn
100 105 110

Cys Cys Gly Leu Lys Glu Ser Gln Ile Leu Ser Leu Leu Ser Asp Ile
115 120 125

Gly Ser Gly Ile Arg Tyr Leu His Glu Asn Lys Ile Ile His Arg Asp
130 135 140

Leu Lys Pro Glu Asn Ile Val Leu Gln Asp Val Gly Gly Lys Ile Ile
145 150 155 160

His Lys Ile Ile Asp Leu Gly Tyr Ala Lys Asp Val Asp Gln Gly Ser
165 170 175

Leu Cys Thr Ser Phe Val Gly Thr Leu Gln Tyr Leu Ala Pro Glu Leu
180 185 190

Phe Glu Asn Lys Pro Tyr Thr Ala Thr Val Asp Tyr Trp Ser Phe Gly
195 200 205

Thr Met Val Phe Glu Cys Ile Ala Gly Tyr Arg Pro Phe Leu His His
210 215 220

Leu Gln Pro Phe Thr Trp His Glu Lys Ile Lys Lys Lys Asp Pro Lys
 225 230 235 240

Cys Ile Phe Ala Cys Glu Glu Met Ser Gly Glu Val Arg Phe Ser Ser
 245 250 255

His Leu Pro Gln Pro Asn Ser Leu Cys Ser Leu Ile Val Glu Pro Met
 260 265 270

Glu Asn Trp Leu Gln Leu Met Leu Asn Trp Asp Pro Gln Gln Arg Gly
 275 280 285

Gly Pro Val Asp Leu Thr Leu Lys Gln Pro Arg Cys Phe Val Leu Met
 290 295 300

Asp His Ile Leu Asn Leu Lys Ile Val His Ile Leu Asn Met Thr Ser
 305 310 315 320

Ala Lys Ile Ile Ser Phe Leu Leu Pro Pro Asp Glu Ser Leu His Ser
 325 330 335

Leu Gln Ser Arg Ile Glu Arg Glu Thr Gly Ile Asn Thr Gly Ser Gln
 340 345 350

Glu Leu Leu Ser Glu Thr Gly Ile Ser Leu Asp Pro Arg Lys Pro Ala
 355 360 365

Ser Gln Cys Val Leu Asp Gly Val Arg Gly Cys Asp Ser Tyr Met Val
 370 375 380

Tyr Leu Phe Asp Lys Ser Lys Thr Val Tyr Glu Gly Pro Phe Ala Ser
 385 390 395 400

Arg Ser Leu Ser Asp Cys Val Asn Tyr Ile Val Gln Asp Ser Lys Ile
 405 410 415

Gln Leu Pro Ile Ile Gln Leu Arg Lys Val Trp Ala Glu Ala Val His
 420 425 430

Tyr Val Ser Gly Leu Lys Glu Asp Tyr Ser Arg Leu Phe Gln Gly Gln
 435 440 445

Arg Ala Ala Met Leu Ser Leu Leu Arg Tyr Asn Ala Asn Leu Thr Lys
 450 455 460

Met Lys Asn Thr Leu Ile Ser Ala Ser Gln Gln Leu Lys Ala Lys Leu
 465 470 475 480

Glu Phe Phe His Lys Ser Ile Gln Leu Asp Leu Glu Arg Tyr Ser Glu
 485 490 495

Gln Met Thr Tyr Gly Ile Ser Ser Glu Lys Met Leu Lys Ala Trp Lys
 500 505 510

Glu Met Glu Glu Lys Ala Ile His Tyr Ala Glu Val Gly Val Ile Gly
 515 520 525

Tyr Leu Glu Asp Gln Ile Met Ser Leu His Ala Glu Ile Met Glu Leu
 530 535 540

Gln Lys Ser Pro Tyr Gly Arg Arg Gln Gly Asp Leu Met Glu Ser Leu
 545 550 555 560

Glu Gln Arg Ala Ile Asp Leu Tyr Lys Gln Leu Lys His Arg Pro Ser
 565 570 575

Asp His Ser Tyr Ser Asp Ser Thr Glu Met Val Lys Ile Ile Val His
 580 585 590

Thr Val Gln Ser Gln Asp Arg Val Leu Lys Glu Leu Phe Gly His Leu
 595 600 605

Ser Lys Leu Leu Gly Cys Lys Gln Lys Ile Ile Asp Leu Leu Pro Lys
 610 615 620

Val Glu Val Ala Leu Ser Asn Ile Lys Glu Ala Asp Asn Thr Val Met
 625 630 635 640

Phe Met Gln Gly Lys Arg Gln Lys Glu Ile Trp His Leu Leu Lys Ile
 645 650 655

Ala Cys Thr Gln Ser Ser Ala Arg Ser Leu Val Gly Ser Ser Leu Glu
 660 665 670

Gly Ala Val Thr Pro Gln Thr Ser Ala Trp Leu Pro Pro Thr Ser Ala
 675 680 685

Glu His Asp His Ser Leu Ser Cys Val Val Thr Pro Gln Asp Gly Glu

690		695		700
Thr Ser Ala Gln Met Ile Glu Glu Asn Leu Asn Cys Leu Gly His Leu				
705		710		715 720
Ser Thr Ile Ile His Glu Ala Asn Glu Glu Gln Gly Asn Ser Met Met				
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Asn Leu Asp Trp Ser Trp Leu Thr Glu				
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Met Arg Glu Arg Leu Gly Thr Gly Gly Phe Gly Asn Val Cys Leu Tyr				
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Gln His Arg Glu Leu Asp Leu Lys Ile Ala Ile Ala Ser Cys Arg Leu				
	35		40	45
Glu Leu Ser Thr Lys Asn Arg Glu Arg Trp Cys His Glu Ile Gln Ile				
	50		55	60
Met Lys Lys Leu Asn His Ala Asn Val Val Lys Ala Cys Asp Val Pro				
65	70		75	80
Glu Glu Leu Asn Ile Leu Ile His Asp Val Pro Leu Leu Ala Met Glu				
	85		90	95
Tyr Cys Ser Gly Gly Asp Leu Arg Lys Leu Leu Asn Lys Pro Glu Asn				
	100		105	110
Cys Cys Gly Leu Lys Glu Ser Gln Ile Leu Ser Leu Leu Ser Asp Ile				
	115		120	125
Gly Ser Gly Ile Arg Tyr Leu His Glu Asn Lys Ile Ile His Arg Asp				
	130		135	140

Leu Lys Pro Glu Asn Ile Val Leu Gln Asp Val Gly Gly Lys Ile Ile
 145 150 155 160

His Lys Ile Ile Asp Leu Gly Tyr Ala Lys Asp Val Asp Gln Gly Ser
 165 170 175

Leu Cys Thr Ser Phe Val Gly Thr Leu Gln Tyr Leu Ala Pro Glu Leu
 180 185 190

Phe Glu Asn Lys Pro Tyr Thr Ala Thr Val Asp Tyr Trp Ser Phe Gly
 195 200 205

Thr Met Val Phe Glu Cys Ile Ala Gly Tyr Arg Pro Phe Leu His His
 210 215 220

Leu Gln Pro Phe Thr Trp His Glu Lys Ile Lys Lys Lys Asp Pro Lys
 225 230 235 240

Cys Ile Phe Ala Cys Glu Glu Met Ser Gly Glu Val Arg Phe Ser Ser
 245 250 255

His Leu Pro Gln Pro Asn Ser Leu Cys Ser Leu Ile Val Glu Pro Met
 260 265 270

Glu Asn Trp Leu Gln Leu Met Leu Asn Trp Asp Pro Gln Gln Arg Gly
 275 280 285

Gly Pro Val Asp Leu Thr Leu Lys Gln Pro Arg Cys Phe Val Leu Met
 290 295 300

Asp His Ile Leu Asn Leu Lys Ile Val His Ile Leu Asn Met Thr Ser
 305 310 315 320

Ala Lys Ile Ile Ser Phe Leu Leu Pro Pro Asp Glu Ser Leu His Ser
 325 330 335

Leu Gln Ser Arg Ile Glu Arg Glu Thr Gly Ile Asn Thr Gly Ser Gln
 340 345 350

Glu Leu Leu Ser Glu Thr Gly Ile Ser Leu Asp Pro Arg Lys Pro Ala
 355 360 365

Ser Gln Cys Val Leu Asp Gly Val Arg Gly Cys Asp Ser Tyr Met Val

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			Tyr	Glu 395
			Gly	Pro
			Phe	Ala
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Arg	Ser	Leu	Ser	Asp 405
			Cys	Val
			Asn	Tyr 410
			Ile	Val
			Gln	Asp
			Ser	Lys 415
			Ile	
Gln	Leu	Pro	Ile 420	Ile
			Gln	Leu
			Arg	Lys 425
			Val	Trp
			Ala	Glu
			Ala	Val 430
			His	
Tyr	Val	Ser	Gly	Leu 435
			Lys	Glu
			Asp	Tyr 440
			Ser	Arg
			Leu	Phe 445
			Gln	Gly
			Gln	
Arg	Ala	Ala	Met	Leu 450
			Ser	Leu
			Leu	Arg 455
			Tyr	Asn
			Ala	Asn 460
			Leu	Thr
			Lys	
Met	Lys	Asn	Thr	Leu 465
			Ile	Ser
			Ala	Ser 470
			Gln	Gln 475
			Leu	Lys
			Ala	Lys 480
			Leu	
Glu	Phe	Phe	His	Lys 485
			Ser	Ile
			Gln	Leu 490
			Asp	Leu
			Glu	Arg
			Tyr	Ser 495
			Glu	
Gln	Met	Thr	Tyr	Gly 500
			Ile	Ser
			Ser	Glu 505
			Lys	Met
			Leu	Lys 510
			Ala	Trp
			Lys	
Glu	Met	Glu	Glu	Lys 515
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			His	Tyr 520
			Ala	Glu
			Val	Gly 525
			Val	Ile
			Gly	
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			Ser	Leu 535
			His	Ala
			Glu	Ile 540
			Met	Glu
			Leu	
Gln	Lys	Ser	Pro	Tyr 545
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			Gly	Asp 555
			Leu	Met
			Glu	Ser 560
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			Asp	Leu
			Tyr	Lys 570
			Gln	Leu
			Lys	His
			Arg	Pro 575
			Ser	
Asp	His	Ser	Tyr	Ser 580
			Asp	Ser
			Thr	Glu 585
			Met	Val
			Lys	Ile 590
			Ile	Val
			His	
Thr	Val	Gln	Ser	Gln 595
			Asp	Arg
			Val	Leu 600
			Lys	Glu
			Leu	Phe 605
			Gly	His
			Leu	

Ser Lys Leu Leu Gly Cys Lys Gln Lys Ile Ile Asp Leu Leu Pro Lys
610 615 620

Val Glu Val Ala Leu Ser Asn Ile Lys Glu Ala Asp Asn Thr Val Met
625 630 635 640

Phe Met Gln Gly Lys Arg Gln Lys Glu Ile Trp His Leu Leu Lys Ile
645 650 655

Ala Cys Thr Gln Ser Ser Ala Arg Ser Leu Val Gly Ser Ser Leu Glu
660 665 670

Gly Ala Val Thr Pro Gln Thr Ser Ala Trp Leu Pro Pro Thr Ser Ala
675 680 685

Glu His Asp His Ser Leu Ser Cys Val Val Thr Pro Gln Asp Gly Glu
690 695 700

Thr Ser Ala Gln Met Ile Glu Glu Asn Leu Asn Cys Leu Gly His Leu
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Ser Thr Ile Ile His Glu Ala Asn Glu Glu Gln Gly Asn Ser Met Met
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Asn Leu Asp Trp Ser Trp Leu Thr Glu
740 745

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Gln Arg Glu Asn Pro Pro Gly Pro Pro Ile Ala Ala Ser Ala Pro Gly
35 40 45

Pro Ser Gln Ser Leu Gly Leu Asn Val His Asn Met Thr Pro Ala Thr
50 55 60

Ser Pro Ile Gly Ala Ser Gly Val Ala His Arg Ser Gln Ser Ser Glu
 65 70 75 80

Gly Val Ser Ser Leu Ser Ser Ser Pro Ser Asn Ser Leu Glu Thr Gln
 85 90 95

Ser Gln Ser Leu Ser Arg Ser Gln Ser Met Asp Ile Asp Gly Val Ser
 100 105 110

Cys Glu Lys Ser Met Ser Gln Val Asp Val Asp Ser Gly Ile Glu Asn
 115 120 125

Met Glu Val Asp Glu Asn Asp Arg Arg Glu Lys Arg Ser Leu Ser Asp
 130 135 140

Lys Glu Pro Ser Ser Gly Pro Glu Val Ser Glu Glu Gln Ala Leu Gln
 145 150 155 160

Leu Val Cys Lys Ile Phe Arg Val Ser Trp Lys Asp Arg Asp Arg Asp
 165 170 175

Val Ile Phe Leu Ser Ser Leu Ser Ala Gln Phe Lys Gln Asn Pro Lys
 180 185 190

Glu Val Phe Ser Asp Phe Lys Asp Leu Ile Gly Gln Ile Leu Met Glu
 195 200 205

Val Leu Met Met Ser Thr Gln Thr Arg Asp Glu Asn Pro Phe Ala Ser
 210 215 220

Leu Thr Ala Thr Ser Gln Pro Ile Ala Ala Ala Arg Ser Pro Asp
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Arg Asn Leu Leu Leu Asn Thr Gly Ser Asn Pro Gly Thr Ser Pro Met
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Phe Cys Ser Val Ala Ser Phe Gly Ala Ser Ser Leu Ser Ser Leu Gly
 260 265 270

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 275 280 285

Ile Glu Thr Cys Lys Glu Thr Asp Met Leu Asn Tyr Leu Ile Glu Cys
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Phe Asp Arg Val Gly Ile Glu Glu Lys Lys Ala Pro Lys Met Cys Ser
 305 310 315 320

Gln Pro Ala Val Ser Gln Leu Leu Ser Asn Ile Arg Ser Gln Cys Ile
 325 330 335

Ser His Thr Ala Leu Val Leu Gln Gly Ser Leu Thr Gln Pro Arg Ser
 340 345 350

Leu Gln Gln Pro Ser Phe Leu Val Pro Tyr Met Leu Cys Arg Asn Leu
 355 360 365

Pro Tyr Gly Phe Ile Gln Glu Leu Val Arg Thr Thr His Gln Asp Glu
 370 375 380

Glu Val Phe Lys Gln Ile Phe Ile Pro Ile Leu Gln Gly Leu Ala Leu
 385 390 395 400

Ala Ala Lys Glu Cys Ser Leu Asp Ser Asp Tyr Phe Lys Tyr Pro Leu
 405 410 415

Met Ala Leu Gly Glu Leu Cys Glu Thr Lys Phe Gly Lys Thr His Pro
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Val Cys Asn Leu Val Ala Ser Leu Arg Leu Trp Leu Pro Lys Ser Leu
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Ser Pro Gly Cys Gly Arg Glu Leu Gln Arg Leu Ser Tyr Leu Gly Ala
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Lys Tyr Phe Ser Gly Pro Ala Ile Thr Leu Glu Asn Thr Arg Val Val
 485 490 495

Ser Gln Ser Leu Gln His Tyr Leu Glu Leu Gly Arg Gln Glu Leu Phe
 500 505 510

Lys Ile Leu His Ser Ile Leu Leu Asn Gly Glu Thr Arg Glu Ala Ala
 515 520 525

Leu Ser Tyr Met Ala Ala Val Val Asn Ala Asn Met Lys Lys Ala Gln
 530 535 540

Met Gln Thr Asp Asp Arg Leu Val Ser Thr Asp Gly Phe Met Leu Asn
 545 550 555 560

Phe Leu Trp Val Leu Gln Gln Leu Ser Thr Lys Ile Lys Leu Glu Thr
 565 570 575

Val Asp Pro Thr Tyr Ile Phe His Pro Arg Cys Arg Ile Thr Leu Pro
 580 585 590

Asn Asp Glu Thr Arg Val Asn Ala Thr Met Glu Asp Val Asn Asp Trp
 595 600 605

Leu Thr Glu Leu Tyr Gly Asp Gln Pro Pro Phe Ser Glu Pro Lys Phe
 610 615 620

Pro Thr Glu Cys Phe Phe Leu Thr Leu His Ala His His Leu Ser Ile
 625 630 635 640

Leu Pro Ser Cys Arg Arg Tyr Ile Arg Arg Leu Arg Ala Ile Arg Glu
 645 650 655

Leu Asn Arg Thr Val Glu Asp Leu Lys Asn Asn Glu Ser Gln Trp Lys
 660 665 670

Asp Ser Pro Leu Ala Thr Arg His Arg Glu Met Leu Lys Arg Cys Lys
 675 680 685

Thr Gln Leu Lys Lys Leu Val Arg Cys Lys Ala Cys Ala Asp Ala Gly
 690 695 700

Leu Leu Asp Glu Ser Phe Leu Arg Arg Cys Leu Asn Phe Tyr Gly Leu
 705 710 715 720

Leu Ile Gln Leu Leu Leu Arg Ile Leu Asp Pro Ala Tyr Pro Asp Ile
 725 730 735

Thr Leu Pro Leu Asn Ser Asp Val Pro Lys Val Phe Ala Ala Leu Pro
 740 745 750

Glu Phe Tyr Val Glu Asp Val Ala Glu Phe Leu Phe Phe Ile Val Gln
 755 760 765

Tyr Ser Pro Gln Ala Leu Tyr Glu Pro Cys Thr Gln Asp Ile Val Met

770		775		780
Phe 785	Leu 785	Val 785	Val 785	Met 785
	Leu 790	Cys 790	Asn 790	Gln 790
	Asn 795	Tyr 795	Ile 795	Arg 795
	Asn 800	Pro 800	Tyr 800	
Leu 805	Val 805	Ala 805	Lys 805	
	Leu 810	Val 810	Glu 810	Met 810
	Phe 815	Met 815	Thr 815	Asn 815
	Pro 815	Ala 815	Val 815	
Gln 820	Pro 820	Arg 820	Thr 820	
	Gln 825	Lys 825	Phe 825	Phe 825
	Glu 830	Met 830	Ile 830	Glu 830
	Asn 835	His 835	Pro 835	Leu 835
Ser 835	Thr 835	Lys 835	Leu 835	Leu 835
	Val 840	Pro 840	Ser 840	Leu 840
	Met 845	Lys 845	Phe 845	Tyr 845
	Thr 845	Asp 845	Val 845	
Glu 850	His 850	Thr 850	Gly 850	Ala 850
	Thr 855	Ser 855	Glu 855	Phe 855
	Tyr 860	Asp 860	Lys 860	Phe 860
	Thr 860	Ile 860	Arg 860	
Tyr 865	His 865	Ile 865	Ser 865	Thr 865
	Ile 870	Phe 870	Lys 870	Ser 870
	Leu 875	Trp 875	Gln 875	Asn 875
	Ile 880	Ala 880	His 880	
His 885	Gly 885	Thr 885	Phe 885	Met 885
	Glu 890	Glu 890	Phe 890	Asn 890
	Ser 895	Gly 895	Lys 895	Gln 895
	Phe 895	Val 895	Arg 895	
Tyr 900	Ile 900	Asn 900	Met 900	Leu 900
	Ile 905	Asp 905	Thr 905	Thr 905
	Phe 910	Leu 910	Leu 910	Asp 910
	Glu 915	Ser 915		
Leu 915	Glu 915	Ser 915	Leu 915	Lys 915
	Arg 920	Ile 920	His 920	Glu 920
	Val 925	Gln 925	Glu 925	Glu 925
	Met 930	Lys 930	Asn 930	
Lys 930	Glu 930	Gln 930	Trp 930	Asp 930
	Gln 935	Leu 935	Pro 935	Arg 935
	Asp 940	Gln 940	Gln 940	Ala 940
	Arg 945	Gln 945	Ala 945	Leu 945
Ser 945	Gln 945	Leu 945	Ala 945	Gln 945
	Asp 950	Glu 950	Arg 950	Val 950
	Ser 955	Arg 955	Ser 955	Tyr 955
	Leu 960	Ala 960	Leu 960	
Ala 965	Thr 965	Glu 965	Thr 965	Val 965
	Asp 970	Met 970	Phe 970	His 970
	Ile 975	Leu 975	Thr 975	Lys 975
	Gln 975	Val 975	Gln 975	
Lys 980	Pro 980	Phe 980	Leu 980	Arg 980
	Pro 985	Glu 985	Leu 985	Gly 985
	Pro 990	Arg 990	Leu 990	Ala 990
	Ala 995	Met 995	Leu 995	
Asn 995	Phe 995	Asn 995	Leu 995	Gln 995
	Gln 1000	Cys 1000	Gly 1000	Pro 1000
	Lys 1005	Cys 1005	Arg 1005	Asp 1005
	Leu 1005	Lys 1005		

Val	Glu	Asn	Pro	Glu	Lys	Tyr	Gly	Phe	Glu	Pro	Lys	Lys	Leu	Leu
1010						1015					1020			
Asp	Gln	Leu	Thr	Asp	Ile	Tyr	Leu	Gln	Leu	Asp	Cys	Ala	Arg	Phe
1025						1030					1035			
Ala	Lys	Ala	Ile	Ala	Asp	Asp	Gln	Arg	Ser	Tyr	Ser	Lys	Glu	Leu
1040						1045					1050			
Phe	Glu	Glu	Val	Ile	Ser	Lys	Met	Arg	Lys	Ala	Gly	Ile	Lys	Ser
1055						1060					1065			
Thr	Ile	Ala	Ile	Glu	Lys	Phe	Lys	Leu	Leu	Ala	Glu	Lys	Val	Glu
1070						1075					1080			
Glu	Ile	Val	Ala	Lys	Asn	Ala	Arg	Ala	Glu	Ile	Asp	Tyr	Ser	Asp
1085						1090					1095			
Ala	Pro	Asp	Glu	Phe	Arg	Asp	Pro	Leu	Met	Asp	Thr	Leu	Met	Thr
1100						1105					1110			
Asp	Pro	Val	Arg	Leu	Pro	Ser	Gly	Thr	Ile	Met	Asp	Arg	Ser	Ile
1115						1120					1125			
Ile	Leu	Arg	His	Leu	Leu	Asn	Ser	Pro	Thr	Asp	Pro	Phe	Asn	Arg
1130						1135					1140			
Gln	Thr	Leu	Thr	Glu	Ser	Met	Leu	Glu	Pro	Val	Pro	Glu	Leu	Lys
1145						1150					1155			
Glu	Gln	Ile	Gln	Ala	Trp	Met	Arg	Glu	Lys	Gln	Asn	Ser	Asp	His
1160						1165					1170			